REMARKS

Claims 1-15 were rejected in the non-final Office Action and Claims 16-41 were withdrawn by the Examiner as being drawn to nonelected subject matter. Claims 1, 16, and 19 have been amended, Claims 2, 4, 17, 18, and 32-41 have been canceled without prejudice.

Claim 1 has been amended to recite that "the packed bed apparatus contains a packing material selected from the group consisting of metal, ceramic, plastic and glass, and wherein the packing material is spherical beads ranging in size from 20 to 1000 μm." Support for this amendment can be found at paragraphs 0049 and 0050 of the as-filed application, and in Claims 2, 17, 37, and 39-41. Claim 16 has been likewise amended. As a result of the amendments to Claims 1 and 16, Claims 2, 4, 17, and 18 and have been canceled, without prejudice. Claims 32-41 have also been canceled, without prejudice.

No new matter has been added by these amendments; therefore, examination is requested to continue on the claims as amended herewith.

Rejection under 35 U.S.C. § 103

In the Office Action, the Examiner rejected Claim 1-15 under 35 U.S.C. § 103(a) as allegedly being obvious over U.S. Patent 6,379,704 to Wright (hereinafter "Wright") in view of U.S. Patent 4,183,681 to Li (hereinafter "Li") and U.S. Application Publication 2002/0025329 to O'Hagan (hereinafter "O'Hagan"). Applicants respectfully traverse this rejection to the extent that it may apply to the claims as amended herewith.

The Examiner referred to Example 3 in Wright, which discloses a method of making naltrexone containing PLGA microcapsules. While there are other differences in the method of Wright as compared to the claims, the Examiner correctly identified one difference as being the absence of any disclosure in Wright about the use of a packed bed apparatus under laminar flow conditions for forming an emulsion. For this missing feature, the Examiner cited Li.

Li does disclose a packed bed apparatus for forming emulsions. However, Li teaches that its packed bed apparatus is operated under turbulent conditions (*i.e.*, not under laminar flow conditions as is recited in the claims). *See* for example Li at Tables II, III, VII, and VIII, where very high flow rates and shear rates disclosed. In fact, nowhere in text of Li is there mention of "laminar" or "non-turbulent" conditions. Laminar flow conditions are simply not disclosed anywhere in Li, and such conditions cannot be inferred from this reference. So the Examiner's statements in the Office Action that Li teaches the use of a packed bed apparatus under laminar

flow conditions is not correct. As such, even if the skilled artisan were to combine Wright with Li as the Examiner alleged, the combination would not result in the claimed method.

Additionally, Li does not teach the use of spherical beads, let alone spherical beads ranging in size from 20-1000 μm. Li only discloses various irregularly shaped packing material such as metal sponges or shavings, ceramic chips, animal hair, plastic brush, tubes, and "C-shaped" Cannon packing material (col. 3, ll. 3-22). In fact, Li states that perforated glass beads "will not work" (col. 3, lines23-25). Accordingly, there is nothing in Li to direct the skilled artisan to using a packed bed apparatus under non-turbulent (laminar) flow conditions, much less a packed bed apparatus with the spherical beads from 20-1000 μm under non-turbulent conditions.

Still further, it is generally unexpected to get sufficient mixing so as to form a good emulsion at non-turbulent (laminar) flow conditions. To the contrary, it is generally accepted that emulsification requires high-shear mixing using systems that have turbulent flow conditions (high Reynolds number values). The specification, however, discusses the unexpected and significant effects provided by a packed bed mixer operating at non-turbulent (laminar) flow rates, thereby allowing the production of high-quality microparticles (*see* paragraphs 0040 and 0044). The use of low shear mixing or laminar flow, which is the opposite of that taught in Li, translates into a typical Reynolds number of less than 10. This is nearly 10 times or more below the Reynolds number for high shear, turbulent flows characteristic of methods like Li's. Thus, the use of laminar flow to form an emulsion is antithetical to the general understanding in the art.

Applicants have developed, however, a method whereby one can obtain high quality microcapsules using laminar flow rates. Such effects are obtained when the diameter of the spherical beads of the packed bed mixer ranges from 20 to 2000 μm (*see* paragraph 0050). Moreover, the unique dynamics of the packed bed mixer allows for the production of microparticles continuously at very low flow rates, which is not possible with other mixing devices. The low flow rate enables the consistent production of high-quality microparticles as small as 0.1 grams that maintain consistent particle size distribution (*see* paragraph 0051). Furthermore, the flow dynamics of the packed bed apparatus of the claimed invention provides for scalability from laboratory to manufacturing sized batches. This cannot be done with a turbulent mixer as in Li (*see* paragraph 0009). Also provided by the claimed method is reproducibility and narrow particle size distribution, which is very difficult to obtain when using

the turbulent conditions taught in Li (*see* paragraphs 0006-0007). So not only was laminar flow not expected to work for forming emulsions and microcapsules, it was certainly not expected to work well.

In summary, even if the skilled artisan were to combine the teachings of Wright and Li, and thus use the particular packed bed apparatus and conditions of Li in Wright's method of making microcapsules, the combination would not result in the claimed methods. Indeed, the claimed method uses a nearly opposite flow and shear regime as that taught in Li. As such, the rejection under section 103 should be withdrawn.

It is noted that the reference to O'Hagan is to simply supply another teaching about a general microencapsulation method and a teaching about the use of emulsion stabilizers such as PVA. This teaching, when combined with Wright and/or Li, does not remedy the deficiencies in the above rejection. So the claims are patentable over the combination of Wright, Li, and O'Hagan for the same reasons noted above.

Claim 11 was further rejected as being obvious over the combination of Wright, Li, O'Hagan, in further view of U.S. Application Publication No. 2002/0028216 to Donovan (hereinafter "Donovan") and U.S. Patent 5,846,562 to Yani (hereinafter "Yani"). Here, the Examiner relied on the combination of Wright, Li, and O'Hagan as mentioned above, but acknowledged that the combination failed to disclose the use of albumin as an emulsion stabilizer. For this missing feature the Examiner cited Donovan and Yani, which mention albumin as an emulsion stabilizer. But as noted above, the combination of references still fails to disclose the use of a particular packed bed apparatus operating under laminar flow conditions. None of the cited references teach this feature (contrary to the Examiner's original assumptions). Moreover, Applicants have demonstrated results that were quite unexpected, given than non-turbulent conditions were not thought to be able to provide sufficient emulsion formation. Thus, for similar reasons noted above, Claim 11 is not obvious over the combination of 5 different references cited by the Examiner.

Lastly, since the withdrawn claims (Claims 16, and 19-31) likewise recite the features of a particular packed bed column operating under laminar flow conditions, these claims are patentable over the cited references and should be rejoined.

CONCLUSION

Enclosed herewith is payment in the amount of $425.00, which includes the $245.00 fee under 37.C.F.R. §1.17(a)(2) for the Two-Month Extension of Time and the $180.00 fee under 37 C.F.R. § 1.17(p) for the Supplemental Information Disclosure Statement. No additional fees are believed due; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,
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/Christopher L. Curfman/	April 14, 2010
Christopher L. Curfman	Date